Claims

1. A method for detecting an infection of an acid-resistant microorganism, wherein

(a) a stool sample of a mammal is incubated with at least two different monoclonal antibodies, fragments or derivatives thereof or aptamers under conditions allowing a complex formation of antigens from the acid-resistant microorganisms with the antibodies, fragments or derivatives thereof or the aptamers and wherein

(aa) the first monoclonal antibody or the fragment or derivative thereof or the first aptamer specifically binds an epitope of the first antigen, which shows at least with some mammals a structure after the intestinal passage that corresponds to the native structure or the structure which a mammal produces antibodies against after being infected or immunised with the acid-resistant microorganism or an extract or lysate thereof or a protein therefrom or a fragment thereof or a synthetic peptide,

(ab) the second monoclonal antibody or the fragment or derivative thereof or the second aptamer specifically binds an epitope of a second antigen differing from the epitope of the first antigen, which shows at least with some mammals a structure after the intestinal passage that corresponds to the native structure or the structure which a mammal produces antibodies against after being infected or immunised with the acid-resistant microorganism or an extract or lysate thereof or a protein therefrom or a fragment thereof or a synthetic peptide,

wherein the groups of mammals may overlap according to (aa) and (ab) and in total essentially make up the overall number of infected mammals; and

(b) the formation of at least one antigen-antibody complex or antigen-aptamer complex according to (aa) or (ab) is detected.

2. A method according to claim 1, wherein the microorganism is an acid-resistant bacterium.

3. A method according to claim 2, wherein the acid-resistant bacterium is a bacterium belonging to the genus Helicobacter or the genus Mycobacterium or the genus Campylobacter.

4. A method according to claim 3, wherein the bacterium is a bacterium belonging to the species *Helicobacter pylori* or *Helicobacter hepaticus* or the species *Mycobacterium tuberculosis* or the species *Campylobacter jejuni* or *Campylobacter pylori*.

5. A method according to claims 1 to 4, wherein the epitope of the first antigen is an epitope of a urease and the epitope of the second antigen is an epitope of a heat shock protein, an alkylhydroperoxide-reductase or of the 20kDa-protein (3-dehydro-quinase type II), the 16.9kDa-protein (neutrophil-activating protein) or the 33.8kDa protein (fructose-bisphosphate-aldolase).

6. A method according to claim 5, wherein the urease is the ß-urease of *H.pylori*.

7. A method according to claims 5 or 6, wherein the heat shock protein is a Hsp60.

8. A method according to any one of claims 5 to 7, wherein the alkylhydroperoxide-reductase is the 26kDa-protein of *H.pylori*.

9. A method according to any one of claims 1 to 8, wherein

(a) a stool sample of a mammal is incubated with three different monoclonal antibodies, fragments or derivatives thereof or aptamers under conditions allowing the complex formation of antigens from the acid-resistant microorganism with antibodies, fragments thereof or derivatives or the aptamers and wherein

(aa) the first monoclonal antibody or the fragment or the derivative thereof or the first aptamer specifically binds an epitope of the first

antigen, which shows at least with some mammals a structure after the intestinal passage that corresponds to the native structure or the structure which a mammal produces antibodies against after being infected or immunised with the acid-resistant microorganism or an extract or lysate thereof or a protein therefrom or a fragment thereof or a synthetic peptide,

(ab) the second monoclonal antibody or the fragment or a derivative thereof or the second aptamer specifically binds an epitope of a second antigen differing from the epitope of the first antigen, which shows at least with some mammals a structure after the intestinal passage that corresponds to the native structure or the structure which a mammal produces antibodies against after being infected or immunised with the acid-resistant microorganism or an extract or lysate thereof or a protein therefrom or a fragment thereof or a synthetic peptide, and

(ac) the third monoclonal antibody or the fragment or derivative or the third monoclonal antibody or the fragment or derivative thereof or the third aptamer specifically binds an epitope of a third antigen differing from the epitope of the first and second antigen, which shows at least with some mammals a structure after the intestinal passage that corresponds to the native structure or the structure which a mammal produces antibodies against after being infected or immunised with the acid-resistant microorganism or an extract or lysate thereof or a protein therefrom or a fragment thereof or a synthetic peptide,

wherein the groups of mammals may overlap according to (aa), (ab) and (ac) and in total essentially make up the overall number of infected mammals; and

(b) the formation of at least one antigen-antibody complex or an antigen-aptamer complex according to (aa), (ab) or (ac) is detected.

10. A method according to claim 9, wherein the epitope of the first antigen is an epitope of a urase, preferably of the ß-urease of *H.pylori*, the epitope of the

second antigen is an epitope of a heat shock protein, preferably of Hsp60 of *H.pylori* and the third antigen is an epitope of an alkylhydroperoxide-reductase, preferably of the 26kDa-protein of *H.pylori*, or wherein the epitope of the second and the third antigen is an epitope of a alkylhydroperoxide-reductase or of the 20kDa-protein (3-dehydro-quinase type II), the 16.9kDa-protein (neutrophil-activating protein) or of the 33.8kDa-protein (fructose-bisphosphate-aldolase).

11. A method according to claims 1 to 10, wherein at least one of the monoclonal antibodies or one of the fragments, derivatives or aptamers binds a conformation epitope.

12. A method according to claim 11, wherein all monoclonal antibodies or fragments, derivatives or aptamers bind conformation epitopes.

13. A method for detecting an infection with *Helicobacter pylori* in the stool of a mammal, wherein

(a) a stool sample is incubated with at least two different monoclonal antibodies, fragments, derivatives thereof or aptamers under conditions allowing an antigen-antibody/antigen-aptamer complex formation, wherein

(aa) the first monoclonal antibody, the fragment, the derivative thereof or the first aptamer specifically binds ß-urease or a fragment thereof;

(ab) the second monoclonal antibody, the fragment, the derivative thereof or the second aptamer specifically binds the 26kDa-antigen or a fragment thereof or specifically binds Hsp60 or a fragment thereof; and

(b) the formation of at least one antigen-antibody complex/antigen-aptamer complex according to (aa) or (ab) is detected.

14. A method for detecting an infection with *Helicobacter pylori* in the stool of a mammal, wherein

(a) a stool sample is incubated with at least two different monoclonal antibodies, fragments, derivatives thereof or aptamers under conditions allowing an antigen-antibody/antigen-aptamer complex formation, wherein

(aa) the first monoclonal antibody, the fragment, the derivative thereof or the first aptamer specifically bind ß-urease or a fragment thereof;

(ab) the second monoclonal antibody, the fragment, the derivative thereof or the second aptamer specifically bind Hsp60 or a fragment thereof; and

(ac) the third monoclonal antibody, the fragment, the derivative thereof or the third aptamer specifically binds the 26kDa-antigen or a fragment thereof; and

(b) the formation of at least one antigen-antibody/antigen-aptamer complex according to (aa), (ab) or (ac) is detected.

15. A method according to any one of claims 7 to 14, wherein the Hsp60-specific antibody is an antibody which has been generated by the hybridoma HP16m/2A5-E6-E5 filed with the German Collection of Microorganisms and Cell Cultures (Deutsche Sammlung von Mikroorganismen und Zellkulturen DSMZ) on June 23, 1998 in accordance with the Statutes of the Budapest Treaty under the filing number DSM ACC2356.

16. A method according to any one of claims 8 to 15, wherein the 26kDa-antigen-specific antibody is an antibody generated by the hybridoma HP15m/3E8-D9-D6 filed with the German Collection of Microorganisms and Cell Cultures (Deutsche Sammlung von Mikroorganismen und Zellkulturen DSMZ) on June 23, 1998 in accordance with the Statutes of the Budapest Treaty under the filing number DSM ACC2355.

17. A method according to anyone of claims 6 to 16, wherein the ß-urease-specific antibody is an antibody generated by the hybridomas HP8m/4H5-D4-C9 or HP9.1m/3C2-F8-E2 filed with the German Collection of Microorganisms and Cell Cultures (Deutsche Sammlung von Mikroorganismen und Zellkulturen

DSMZ) on June 23, 1998 in accordance with the Statutes of the Budapest Treaty under the filing numbers DSM ACC2360 or DSM ACC2362.

18. A method according to any one of claims 7 to 17, wherein the heavy chain of the antibody binding an Hsp60-epitope has at least one of the following CDRs, preferably the CDR3 and still more preferably all of the following CDRs:

CDR1: GFSLSRYSVH
CDR2: MIWGGGSTDYNSGLKS
CDR3: NMGGRYPDYFDY

19. A method according to claim 18, wherein the DNA sequence encoding the heavy chain of the antibody has at least one of the following CDRs, preferably the CDR3 and still more preferably all of the three following CDRs:

CDR1: GG GTTCTCATTA TCCAGATATA GTGTACAC
CDR2: ATGATATGGG GTGGTGGAAG CACAGACTAT AATTCAGGTC TCAAATCC
CDR3: AATATG GGGGGTAGGT ACCCGGACTA CTTTGACTAC

20. A method according to any one of claims 7 to 19, wherein the light chain of the antibody binding an Hsp60-Epitope has at least one of the following CDRs, preferably the CDR3 and still more preferably all of the three following CDRs:

CDR1: RASKSVSTSGYSYIH
CDR2: LASNLES
CDR3: QHSRELPLT

21. A method according to claim 20, wherein the DNA sequence encoding the light chain of the antibody has at least one of the following CDRs, preferably the CDR3 and still more preferably all of the three following CDRs:

CDR1: A GGGCCAGCAA GAGTGTCAGT ACATCTGGCT ATAGTTACAT ACAC
CDR2: C TTGCATCCAA CCTAGAATCT
CDR3: CAGC ACAGTAGGGA GCTTCCGCTC ACG.

22. A method according to any one of claims 8 to 21, wherein the heavy chain of the antibody binding a 26kDa-protein has at least one of the following CDRs, preferably the CDR3 and still more preferably all of the three following CDRs:

CDR1: GFTFNSYAMY
CDR2: RIRSKSDNYATYYANSVKD
CDR3: DHDKFPFYYALDY

23. A method according to claim 22, wherein the DNA sequence encoding the heavy chain of the antibody has at least one of the following CDRs, preferably the CDR3 and still more preferably all of the three following CDRs:

CDR1: GG TTTCACCTTC AATTCCTATG CCATGTAC
CDR2: CGCATAAGAA GTAAAAGTGA TAATTATGCA ACATATTATG CCAATTCAGT GAAAGAC
CDR3: GATCATG ATAAGTTTCC TTTTTACTAT GCTCTGGACT AC

24. A method according to any one of claims 8 to 23, wherein an antibody, a fragment or a derivative thereof is used, whereby the light chain of the antibody binding the 26kDa-protein has at least one of the following CDRs, preferably the CDR3 and still more preferably all of the three following CDRs:

CDR1: TASSSVSSSYLH
CDR2: STSNLAS
CDR3: HQYHRSPPT

25. A method according to claim 24, wherein DNA sequence encoding the light chain of the antibody has at least one of the following CDRs, preferably the CDR3 and still more preferably all of the three following CDRs:

CDR1: A CTGCCAGCTC AAGTGTGAGT TCCAGTTACT TGCAC
CDR2: AGCACTTCCA ACCTGGCTTC T
CDR3: CAC CAGTATCATC GTTCCCCACC GACG

26. A method according to any one of claims 6 to 25, wherein the heavy chain of the antibody binding the epitope of the ß-urease has at least one of the

following CDRs, preferably the CDR3 and still more preferably all of the three following CDRs:

CDR1: GFTFSSHFMS
CDR2: SISSGGDSFYPDSLKG
CDR3: DYSWYALDY
or:
CDR1: GYAFSTSWMN
CDR2: RIYPGDGDTNYNGKFKG
CDR3: EDAYYSNPYSLDY

27. A method according to claim 26, wherein the DNA sequence encoding the heavy chain of the antibody has at least one of the following CDRs, preferably the CDR3 and still more preferably all of the three following CDRs:

CDR1: GG CTACGCATTC AGTACCTCCT GGATGAAC
CDR2: CGGATTTATC CTGGAGATGG AGATACTAAC TACAATGGGA AGTTCAAGGG C
CDR3: GAG GATGCCTATT ATAGTAACCC CTATAGTTTG GACTAC
or:
CDR1: GG ATTCACTTTC AGTAGCCATT TCATGTCT
CDR2: TCCATTAGTA GTGGTGGTGA CAGTTTCTAT CCAGACAGTC TGAAGGGC
CDR3: GACTAC TCTTGGTATG CTTTGGACTA C

28. A method according to any one of claims 6 to 27, wherein the light chain of the antibody binding an epitope of the urease has at least one of the following CDRs, preferably the CDR3 and still more preferably all of the three following CDRs:

CDR1: RASQSIGTRIH
CDR2: YGSESIS
CDR3: QQSNTWPLT
or:
CDR1: HASQNINVWLS
CDR2: KASNLHT
CDR3: QQGRSYPLT

29. A method according to claim 28, wherein DNA sequence encoding the light chain of the antibody has at least one of the following CDRs, preferably the CDR3 and still more preferably all of the three following CDRs:

CDR1: A GGGCCAGTCA GAGCATTGGC ACAAGAATAC AC
CDR2: TAT GGTTCTGAGT CTATCTCT
CDR3: CAACAA AGTAATACCT GGCCGCTCAC G
or:
CDR1: C ATGCCAGTCA GAACATTAAT GTTTGGTTAA GC
CDR2: AAG GCTTCCAACT TGCACACA
CDR3: CAACAG GGTCGAAGTT ATCCTCTCAC G

30. A method according to any one of claims 6 to 29, wherein the antibodies in the variable regions of the light and heavy chains have the amino acid sequences depicted in Figures 1 and 2, Figures 3 and 4, Figures 5 and 6 or Figures 7 and 8.

31. A method according to any one of claims 6 to 30, wherein the coding regions of the variable regions of the light and heavy chains have the DNA sequences depicted in Figures 1 and 2, Figures 3 and 4, Figures 5 and 6, Figures 7 and 8.

32. A method according to any one of claims 1 to 31, wherein the following steps are carried out with the stool sample before incubation with the antibodies: (a) resuspension of the stool sample 1:3 to 1:25, preferably approximately 1:10 in resuspension buffer and (b) mixing on a vortex mixer.

33. A method according to any one of claims 1 to 32, wherein the detection of the formation of the at least one antigen-antibody complex/antigen-aptamer complex in step (b) is carried out by means of an immunological method.

34. A method according to any one of claims 1 to 33, wherein the detection of the formation of the at least one antigen-antibody complex/antigen-aptamer complex in step (b) is carried out by means of ELISA, RIA, Western Blot or an immunochromatographic method.

35. A method according to claim 33 or 34, wherein in RIA or ELISA the same antibody or a fragment or derivative thereof or the same aptamer is used for binding to the solid phase as for detecting the epitope.

36. A method according to any one of claims 1 to 35, wherein the antibodies, the fragments or derivatives thereof or the aptamers are fixed to a support.

37. A method according to any one of claims 1 to 36, wherein the monoclonal antibody is an antibody of mouse.

38. A method according to claims 36, wherein the material of the support is a porous material.

39. A method according to claims 36 or 38, wherein the support is a test strip.

40. A method according to claims 39, 38 or 39, wherein the support consists of cellulose or a derivative of cellulose.

41. A method according to any one of claims 1 to 40, wherein the mammal is a human.

42. A monoclonal antibody, fragment or derivative thereof which has a V region that shows a combination of the CDRs described in any one of claims 18 to 29 or which has been generated by a hybridoma described in any one of claims 15 to 17.

43. A monoclonal antibody, fragment or derivative thereof according to claim 42 which has at least one of the V regions shown in Figures 1 to 8.

44. A monoclonal antibody, fragment or derivative thereof according to claims 42 or 43 which is an antibody of mouse or a fragment or a derivative thereof or a chimeric, preferably humanized antibody or a fragment or derivative thereof.

45. An aptamer which specifically binds the same epitope as the monoclonal antibody, the fragment or derivative thereof according to any one of claims 42 to 44.

46. An epitope which is specifically bound by a monoclonal antibody, fragment or derivative thereof according to any one of claims 42 to 44 or by the aptamer according to claim 45.

47. An antibody, fragment or derivative thereof which specifically binds an epitope according to claim 46.

48. A diagnostic composition containing at least two monoclonal antibodies, fragments or derivatives thereof or aptamers as defined in any one of the aforementioned claims, optionally fixed to a support.

49. A test device for the detection of at least one epitope as defined in any one of the aforementioned claims, comprising

(a) at least two monoclonal antibodies, fragments or derivatives thereof or aptamers as defined in any one of the aforementioned claims fixed to a support;

(b) a device for preparing and analyzing stool samples, optionally

(c) a mixture of at least two monoclonal antibodies, fragments or derivatives thereof or aptamers.

50. A test device for the detection of at least one epitope as defined in any one of the aforementioned claims comprising

(a) at least two monoclonal antibodies, fragments or derivatives thereof or aptamers as defined in any one of the aforementioned claims, wherein the antibodies, fragments or derivatives thereof or aptamers are conjugated with colloidal gold, latex particles or other coloring particles the size of which is typically between 5nm and 100nm, preferably between 20nm and 60nm.

(b) a device for preparing and analyzing of stool samples; and optionally

(c) a mixture of at least two monoclonal antibodies, fragments or derivatives thereof or aptamers.

51. A kit comprising

(a) at least two monoclonal antibodies, fragments or derivatives thereof or aptamers as defined in any one of the aforementioned claims, optionally fixed to a support; optionally

(b) a device for preparing and analyzing stool samples; and optionally

(c) a mixture of at least two monoclonal antibodies, fragments or derivatives thereof or aptamers.

52. A composition, preferably of medicaments, comprising at least one of said antibodies or one of said fragments, derivatives or aptamers, optionally combined with a pharmaceutically acceptable support and/or diluent.

53. A package comprising the diagnostic compound according to claim 48, the test device according to claim 49, 50 or the kit according to claim 51.